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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOAN S. STEFFAN, LESLIE M. THOMPSON,
and JAMES LAWRENCE MARSH

Appeal 2009-005999
Application 10/789,518
Technology Center 1600

Decided: March 2, 2010

Before ERIC GRIMES, RICHARD M. LEBOVITZ, and
STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving a claim to a method for treating Huntington's disease by administering a small ubiquitin-like modifier isopeptidase enhancer. The Patent Examiner rejected the claim as lacking enablement. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The Specification states that Huntington's disease (HD) "is caused by an expansion in a polyglutamine (polyQ) repeat in the amino-terminal domain of the protein, Huntingtin (Htt)...." (Spec. 1:15-16). The Specification explains that Htt is stabilized by the covalent attachment of a "small ubiquitin-like modifier," aka SUMO, where SUMO covalently attaches to Htt lysine residues. (*Id.* at 2:15-22 and 3:6-8). According to the Specification, Applicants "have shown [in Drosophila] that a reduction in cellular SUMOylation results in a rescue of photoreceptor neuron degeneration induced by Huntingtin. Therefore, drugs which . . . increase cleavage of SUMO-1 from Huntingtin, may be useful in the treatment of HD." (*Id.* at 3:9-14). Specifically, the Specification states that "[p]otential therapeutic drugs include agents ... which increase the activity of SUMO isopeptidase" (*id.* at 13:30-33).

Claim 19, the only pending claim, is on appeal. Claim 19 reads as follows:

19. A method of treating Huntington's disease in a patient, comprising administering to a patient diagnosed with Huntington's disease a therapeutically effective amount of a small ubiquitin-like modifier isopeptidase enhancer.

The Examiner rejected the claim under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

ENABLEMENT

The Issue

The Examiner's position is that "[t]he specification does not reasonably provide enablement for treating Huntington's disease (HD), in a

patient diagnosed with HD, comprising administering a therapeutically effective, SUMO isopeptidase enhancer." (Ans. 4). In particular, the Examiner found that "the specification does not disclose any methods or working examples . . . comprising administration of any SUMO isopeptidase enhancer." (*Id.* at 5). According to the Examiner, undue experimentation would be required by a skilled artisan to treat patients with HD and "to identify and administer all possible SUMO isopeptidase enhancers." (*Id.* at 5-6).

The Examiner found that relevant literature teaches that SUMO may function as an antagonist to ubiquitin and is useful in protein degradation. (*Id.* at 6). Additionally, the art taught that "SUMO processing enzymes, having isopeptidase activity and belonging to a family of related proteins, have been characterized from humans and yeast." (*Id.*) However, the Examiner found that the prior art did not teach treating HD patients with a deSUMOylation enhancer. (*Id.*) Moreover, the Examiner found that it was well known in the art that HD has proven to be recalcitrant to treatment. (Ans. 6). Therefore, the Examiner concluded that a skilled artisan "would not be able to predict from the instant specification that all possible deSUMOylation enhancers, including SUMO isopeptidase [enhancers], would be able to treat a complex disease like HD," and that undue experimentation would be required to do so. (*Id.*).

The Examiner also found that the instant Specification described using a Drosophila model for HD which, after crossing with the reduced function Drosophila SUMO mutant (smt3), resulted in the suppression of neurodegeneration. (*Id.* at 7-8)(citing Spec. 3:24-27; 27:22-32; Fig 5A). Additionally, the Examiner found that the Specification demonstrated that

decreased levels of SUMOylation results in the lowering of photoreceptor neuron degeneration in the fly model, induced by the Huntingtin gene (Spec. 3:9-12) suggesting that a reduction of SUMO-1 modification may prove to be useful for treatment of HD. (Ans. 8). However, according to the Examiner, testing for treatment of a disease requires conducting studies on non-human mammals that more closely replicate the essential features of the pathophysiology of the disease in humans. (*Id.*). The Examiner found that neither the Specification nor the art taught any methods or working examples indicating administration of a SUMO isopeptidase enhancer for treatment in humans. (*Id.*).

Therefore, the Examiner concluded that due to the large quantity of experimentation necessary to treat HD by administering a SUMO isopeptidase enhancer, the lack of direction/guidance presented in the Specification, the absence of working examples, the complex nature of the invention, the state of the prior art which has yet to determine a suitable model for treatment of HD, and the unpredictability of using invertebrate models for actual treatment in humans, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention. (*Id.* at 8).

Appellants contend that based upon disclosures in the Specification, one of ordinary skill in the art, having read the study results described in the application, would have been without doubt that administering agents known to enhance the activity of SUMO isopeptidases would have had a therapeutic effect on neurodegenerative diseases generally, and HD specifically. (App. Br. 7). In particular, Appellants assert that the Specification and published studies have demonstrated that (a) "'a reduced function smt3 (Drosophila

SUMO) mutant results in a suppression of lethality and of neurodegeneration'" in HD (App Br. 7) ; (b) "that suppression of SUMOylation or enhancement of deSUMOylation reduce polyglutamine toxicity," (App. Br. 7); and "[m]ost significantly" that (c) study results using a HD fly model "shows specifically that decreased SUMOylation decreases neurodegeneration from Huntington's disease" (App. Br. 7). Based on those disclosures, Appellants assert that "it is well-established by both [their] application and the supporting art that increased levels of SUMO isopeptidase acts to enhance deSUMOylation." (App. Br. 7). According to Appellants, "the Examiner has not provided any argument or evidence that would suggest that determining appropriate SUMO isopeptidase enhancers would entail undue experimentation." (App. Br. 8).

Further, Appellants assert that they "have submitted a number of working examples, including data on the efficacy of a SUMO isopeptidase enhancer in treating Huntington's disease in a fly model." (*Id.* at 9). According to Appellants the fact that the Examiner acknowledged that the fly model is "'extensively used for studying different aspects of neurodegenerative diseases'" and "'a cost-effective platform for testing large matrices of drug combinations,'" is sufficient to establish that a skilled artisan "would have considered there to be a 'reasonable correlation' between Appellants' tests and a therapeutic treatment." (*Id.* at 11).

The issue is whether Appellants have shown that the Examiner erred in concluding that an ordinary artisan would have had to resort to undue experimentation to administer a SUMO isopeptidase enhancer.

Findings of Fact

Breadth of the Claim

1. The method of claim 19 is not limited to a specific SUMO isopeptidase enhancer.

Presence of Working Examples

2. The Specification disclosed that "[c]rossing a *Drosophila* model of HD with a *reduced function smt3* (*Drosophila* SUMO) mutant results in suppression of lethality and neurodegeneration." (Spec. 3:24-26; 27:22-32; Fig 5A)(emphasis added).
3. The Specification does not provide a working example wherein a SUMO isopeptidase enhancer is used.

Amount of Direction or Guidance Presented

4. The Specification does not identify a SUMO isopeptidase enhancer.
5. The Specification does not disclose a method of identifying a compound that functions as a SUMO isopeptidase enhancer.
6. The Specification teaches that "a loss in the ability of *Drosophila* cells to sumoylate proteins *in vivo*" results in reduced polyglutamine toxicity. (*See* Spec. 14:15-17).
7. The Specification teaches that "enhancement of the process of deSUMOylation of proteins, may prevent neurodegeneration and death caused by polyglutamine repeat diseases," such as HD. (Spec. 13:20-22).
8. The Specification states that potential therapeutic agents include agents "which increase the activity of SUMO isopeptidase...." (Spec. 13:30-34).

State of the Prior Art and Unpredictability of the Art

9. The Specification disclosed that drugs that can enhance the process of deSUMOylation of proteins "have not been developed and are not available." (Spec. 13:24-26).
10. Wang[1] teaches that "[t]he pathogenesis of HD has not yet been fully understood." (Wang, p. 1287)
11. Wang also teaches that "there is no ideal model which replicates all of the essential features of neuropathology and progressive motor and cognitive impairments of human HD." (Wang Abstract).
12. Melchior[2] teaches that "SUMO modification is reversible." (Melchior, p. 597).
13. Melchior also teaches that "[f]our SUMO C-terminal hydrolases/isopeptidases have now been identified...." (*Id.*).

Principles of Law

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997)(quoting *In re Wright,* 999 F.2d 1557, 1561 (Fed. Cir. 1993)). "Tossing out the mere germ of an idea does not constitute enabling disclosure." *Id.* at 1366.

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[1] Lin-hui Wang et al., *Animal models of Huntington's disease: Implications in uncovering pathogenic mechanisms and developing therapies*, 27 ACTA PHARMACOLOGICA SINICA 1287-1302 (2006).
[2] Frauke Melchior, *SUMO-Nonclassical Ubiquitin*, in 16 ANNU. REV. CELL DEV. BIOL. 591-626 (2000).

"Factors to be considered in determining whether a disclosure would require undue experimentation . . . . include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

"It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed." *In re Vaeck*, 947 F.2d 488, 496 & n. 23 (Fed.Cir.1991) (citation omitted).

Analysis

We agree with the Examiner that the Specification does not provide sufficient guidance to enable practice of the full scope of the claimed invention without undue experimentation. The nature of the invention places it in the class which the Federal Circuit has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant. Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Specification expressly teaches that "[c]rossing a *Drosophila* model of HD with a *reduced function smt3* (*Drosophila* SUMO) mutant results in suppression of lethality and neurodegeneration." (FF2). The Specification also states that "a loss in the ability of Drosophila cells to sumoylate proteins in vivo" resulted in reduced polyglutamine toxicity.

(FF5). Therefore, Appellants suggest in the Specification that "enhancement of the process of deSUMOylation of proteins, may prevent neurodegeneration and death caused by polyglutamine repeat diseases," such as HD. (FF7). In particular, the Specification disclosed that potential therapeutic agents include agents "which increase the activity of SUMO isopeptidase...." (FF8).

However, the Specification does not identify or describe what compound will function as a SUMO isopeptidase enhancer. Contrary to Appellants' assertion that they "have submitted a number of working examples, including data on the efficacy of a SUMO isopeptidase enhancer in treating Huntington's disease in a fly model" (App. Br. 9), the evidence does not support that argument. Our review of the Specification shows that flies were *genetically altered* to express "reduced SUMOylation activity (i.e. heterozygous for a SUMO mutant, smt3/+)" (*see* Spec. at 27:22-32 and Fig. 5a). The study did not involve administration of a SUMO isopeptidase enhancer. The Specification does not provide an example of a SUMO isopeptidase enhancer that can be administered to a patient. We find that a skilled artisan would understand why treating HD by administering a therapeutically effective amount of a SUMO isopeptidase enhancer may be desirable, if such an enhancer were available. However, the evidence is that such enhancers were unknown at the time of filing, and the Specification does not identify or describe one. In other words, Appellants are claiming a theoretical method that would require experimentation to implement. *See Genentech, Inc.*, 108 F.3d at 1367.

While we agree with Appellants that a disclosure need not enable a skilled artisan to identify "all possible" SUMO isopeptidase enhancers as the

Examiner wrote, the Specification must provide sufficient detail to enable a skilled artisan to identify or make at least one agent that will function as a SUMO isopeptidase enhancer. As Appellants acknowledge in the Specification, drugs that can enhance the process of deSUMOylation of proteins, presumably including SUMO isopeptidase enhancers, "have not been developed and are not available." (FF9). We conclude that the artisan would have to perform undue experimentation to discover the agent for use in the method of the invention.

In the Reply, Appellants again emphasize that their Specification and the prior art "make it clear that the function of SUMO isopeptidases as mechanisms to reverse SUMOylation are and have been well-known for some time." (Reply Br. 13). What remains missing is a description of the enhancer in sufficient detail so as to enable a skilled artisan to obtain a SUMO isopeptidase enhancer and use the claimed method of treating HD.

CONCLUSION OF LAW

Appellants have not shown that the Examiner erred in concluding that an ordinary artisan viewing the present Specification would have had to resort to undue experimentation to practice the method recited in claim 19.

SUMMARY

We affirm the rejection of claim 19 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

lp

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